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EXAMINER	
PIHONAK, SARAH	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,744	YOKOZAWA ET AL.	
	Examiner	Art Unit	
	SARAH PIHONAK	4121	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This application is a 371 (national stage application) of PCT/JP2004/017998.

2. Claims 1-18 are pending.

Claim Rejections 35 U.S.C. § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

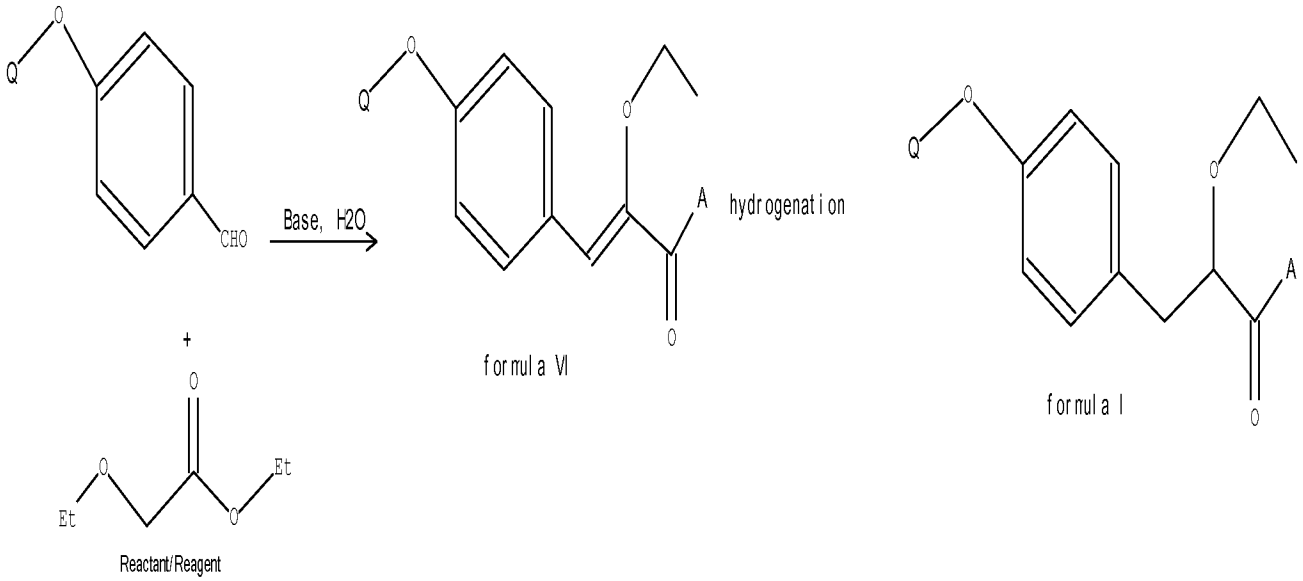
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 7,002,037 patent (US '037) in view of *J. Amer. Chem. Soc.*, **1998**, *120*, 4345-4353.

5. Regarding instant claim 1 of the application, US '037 teaches the following:

The invention disclosed in US '037 is drawn to the preparation of an *(S)*-enantiomer compound of formula I. US '037 was discovered during a search by the examiner for subject matter concerning the current application. The particular reagents used in this example are 4-methoxybenzaldehyde, and ethyl 2-ethoxyethanoate, but is not intended to be limiting, as stated on page 4, column 5, lines 50-53 "The following Examples are intended to illustrate, but in no way limit the scope of the invention". The reaction is performed in the presence of a base in an organic solvent, which is followed

by hydrolysis to give the condensation product, Formula VI , which is further converted to formula I through hydrogenation. At this point, the *(S)*- enantiomer of formula is isolated by use of chiral agents, chiral column chromatography, and crystallization (page 2, column 1, lines 30-67). The *(S-)* enantiomer may also be separated with chiral agents before hydrogenation. Hydrogenation may be performed with Pd/C, or a chiral catalyst (page 4, column 5, lines 23-26). The hydrogenating agent is not limited in the scope of the invention. The invention is drawn to the derivative compound of formula I, in which the substituent on the oxygen β to the carboxyl group is ethyl.

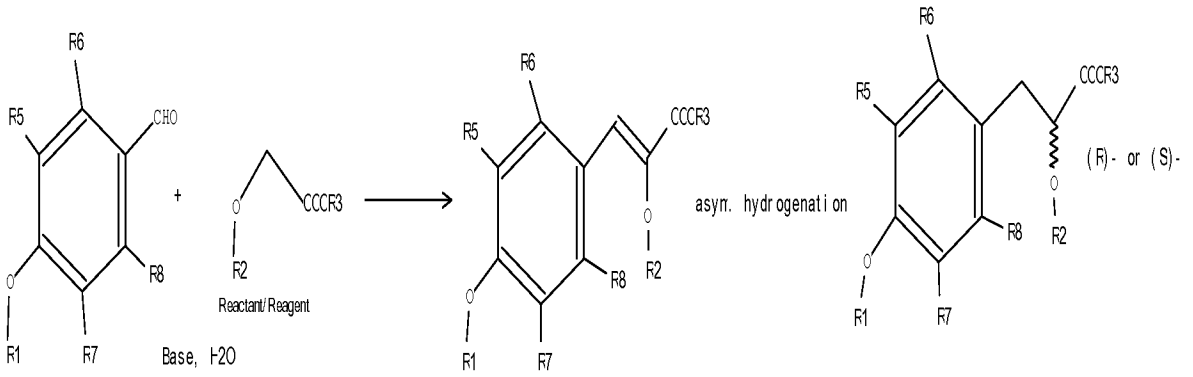


where Q = H, or a protecting group

A = H, or a chiral auxiliary group, or R^p, where R^p = protecting group

Additionally, the phenyl group of Formula I may be substituted by one or more halogen atoms (page 3, column 4, lines 8-39).

Instant claim 1 of the application discloses that a compound of formula (4) is prepared by reaction of a benzaldehyde of formula (1) with a glycolic acid derivative of formula (2). The specification of the application further states that this reaction is accomplished by a base, and a list of possible bases is shown (page 11, paragraph 0109).



Scheme 1 Formula (4)

The applicant has defined the R groups as the following:

R1 = a protecting group; R2 = alkyl group; R3 = hydrocarbon group; R5 – R8 = independently H or a substituent.

Formula VI has essentially the same formula as that of formula (4), in instant claim 1 of the application. The R2 substituent of instant claim 1 is an alkyl group, of which the ethyl substituent of US '037 would be included. The R5-R8 substituents of formula (4) may be either H or another substituent; the phenyl substituents of the formulas present in US '037 may be either H or halogen atoms. R1 of instant claim 1 is initially a protecting group, which is eventually removed; the Q substituent may be either H or a protecting group. The substituent R3 of the instant claim is a hydrocarbon group; in US '037, the A group may be either H, a chiral auxilliary group, or a protecting group. The reaction steps, in which a benzaldehyde and glycolic acid derivative are reacted with a base, followed by hydrolysis, to give the resultant compound of formula I are also identical to the reaction steps in the present application.

Instant claim 1 further states that the formula (4) undergoes asymmetric hydrogenation to form the resulting hydrogenated *(R)* or *(S)* enantiomer. There is not a reference in this claim as to a specific reagent or catalyst to be used for the asymmetric hydrogenation. It is known in the art that the specific (R)- or (S)- enantiomer results from use of a chiral ligand of specific stereochemistry. US '037 teaches that the final compound VIII is prepared by hydrogenation with a catalyst. The catalyst may be Pd/C, or a chiral catalyst ('037, page 4, column 5, lines 23-26). In this example, a chiral catalyst would be used for asymmetric hydrogenation. Therefore, the element of asymmetric hydrogenation is implied by US '037. Following asymmetric hydrogenation, US '037 states that protecting groups may be removed (page 2, column 1, lines 43-55), as also stated in instant claim 1.

6. Instant claim 2 restates the reaction process, in which a benzaldehyde and a glycolic acid derivative, in the presence of a base, followed by hydrolysis (Scheme 1, page 11 of the instant application), provides the compound of formula (4). The derivative of formula (4) further undergoes asymmetric hydrogenation, and removal of protection groups. There is no statement in claim 2 as to the specific reagent or catalyst to be used for the reaction. As stated above, this is identical to what is disclosed in US '037.

7. Instant claim 3 states that the reacting benzaldehyde is a derivative of 4-hydroxybenzaldehyde. The other reaction steps to form the 4-hydroxycinnamic acid of formula (9) are the same as described for instant claims 1 and 2. Claim 3 further states that the derivative of formula (9) undergoes asymmetric hydrogenation. There is no statement in claim 3 as to the specific agent or catalyst to be used for the hydrogenation. As the Q group of Formula I of US '037 may also be H, these components of instant claim 3 are also disclosed by '037.

8. Instant claim 4 recites the process of instant claim 1, and additionally, that the asymmetric hydrogenation is carried out on a chiral catalyst. US '037 states that the hydrogenation can be carried out with a catalyst such as Pd/C, but that the chosen catalyst may be chiral (page 4, column 5, 23-26). All of the components of instant claim 4 are taught by US '037.

9. Instant claim 14 restates that a compound of general formula (4) undergoes asymmetric hydrogenation to form the desired hydrogenated enantiomer. As stated previously, the element of asymmetric hydrogenation is implied by US '037.

10. Instant claim 15 recites that an optically active 3-(4-hydroxyphenyl)propionic acid derivative is prepared by having the 4-hydroxycinnamic acid derivative undergo asymmetric hydrogenation. According to Formula VI of US '037, the Q substituent may also be H, and would also be a 4-hydroxycinnamic acid derivative. Additionally, asymmetric hydrogenation was also previously implied by US '037.

11. Instant claim 16 essentially repeats the process recited in instant claim 15.

12. Instant claim 17 essentially repeats the process recited in instant claims 15 and 16.

13. Instant claim 18 states that a compound of formula (4) would be prepared according to Scheme 1 (shown previously), and that compound (4) would be further subjected to asymmetric hydrogenation to form the desired enantiomeric product, followed by removal of any protection groups. Theses components are also taught by US '037.

14. Regarding instant claim 1, US '037 does not teach the following:

For instant claim 1, the possible substituents for the starting benzaldehyde, and eventually the final product, are very broad. For substituents R5-R8, instant claim 1 recites that the groups may be H or a substituent. For the invention disclosed in US '037, the phenyl ring subsituents may be H or halogen atoms. The R2 group of instant claim 1 is an alkyl group, which would correspond to the specified ethyl group of US '037. As the possible substituents of instant claim 1 are infinitely broad, US '037 does not encompass all of the same substituents.

15. Regarding instant claim 2, the same explanation shown above applies regarding the substituents.

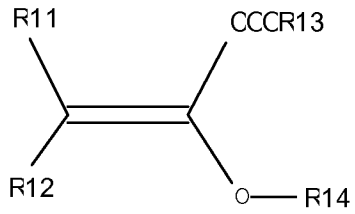
16. Regarding instant claim 3, the same explanation applies regarding substituents.

17. Regarding instant claim 4, the same explanation applies regarding substituents.

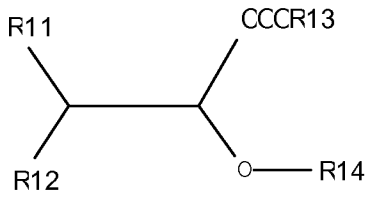
18. Instant claim 5 recites the process as stated in instant claim 1, and additionally, that the chiral catalyst is a transition metal catalyst. This is not stated in US '037.

19. Instant claim 6 recites the process of instant claim 5, and further states, that the metal of the transition metal complex is within Groups 8 to 10 of the periodic table.

20. Instant claim 7 introduces a new reactant compound, shown below:



(11)



(12)

For compounds (11) and (12), the functional groups are defined as follows:

R11, R12 = H or a substituent

R13 = H, or an optionally substituted hydrocarbon group or metal atom

R14 = H or a protective group

Claim 7 recites that compound (12) is prepared by asymmetric hydrogenation of compound (11) with a transition metal complex as catalyst, and additionally, that if the transition metal catalyst is Rh, the R14 group is not acyl. None of these components are taught by US '037.

21. Instant claim 8 recites the process as stated in instant claim 7, and additionally, that the metal of the transition metal complex be within Groups 8 to 10 of the periodic table. This is not taught by US '037.

22. Instant claim 9 recites the process as stated in instant claim 1, as well as, that the chiral catalyst for the hydrogenation is composed of a chiral ligand and a transition metal compound.

23. Instant claim 10 recites the process as stated in claim 1, and also that, the optically active produce is crystallized from a solvent. US '037 does not explicitly state this.

24. Instant claim 11 recites the process as stated in instant claim 10, and also that, the crystallization solvent be selected from hydrocarbons, alcohols, ketones, water, and a mixture thereof. US '037 does not explicitly state this.

25. Instant claim 12 recites the process of claim 1, in which the optically active 3-(4-hydroxyphenyl)propionic acid derivative is crystallized from a solvent. US '037 does not explicitly state this.

26. Instant claim 13 recites the process of instant claim 12, and additionally that, the crystallization solvent is selected form the group consisting of aromatic hydrocarbons, aliphatic hydrocarbons, alcohols, water, and a mixture thereof. US '037 does not explicitly teach this.

27. Instant claim 14 restates that a compound of formula 4 is subjected to asymmetric hydrogenation to form the desired enantiomer product. The possible

variation in different substituents is the only element not completely disclosed in US '037.

28. Instant claim 15 restates the asymmetric hydrogenation of the 4-hydroxy derivative of formula 4. The only element not completely disclosed in US '037 applies to the possible variation of substituents.

29. Instant claim 16 restates the process of instant claim 15. US '037 does not possibly teach all of the same variations of substituents.

30. Instant claim 17 restates the asymmetric hydrogenation of a derivative of formula (4). US '037 does not possibly teach all of the same variations of substituents.

31. Instant claim 18 states that a 4-hydroxyphenyl propionic acid derivative is prepared from a benzaldehyde derivative and a glycolic acid derivative, and then is further subjected to asymmetric hydrogenation and deprotection. US '037 teaches this, but does not disclose all of the same variations of substituents.

32. The subject matter taught in the reference *J. Am. Chem. Soc.* **1998**, *120*, 4345-4353 (hereafter referred to as JACS '98), regarding asymmetric hydrogenation, is considered to be very similar to what is cited in the current application claims. The JACS '98 article was provided by the applicant in the Information Disclosure Statement. In this article, α-alkoxy esters are prepared by asymmetric hydrogenation with a chiral rhodium catalyst, [(*S, S*)-Et-DUPHOS-Rh]$^+$ (Table 3, page 4349, substrates 4i). The desired *(S)*- enantiomer is acquired through application of the *(S,S)*- chiral Et-DUPHOS attached to the rhodium.

For instant claim 1, the JACS ‘98 discloses the element of preparation of an α-alkoxy ester through asymmetric hydrogenation. Regarding the substrates, (Table 3, page 4349, substrate 4i), there is a difference regarding substituents. The phenyl ring of the substrates in JACS ‘98 are not substituted, and do not possess an alkoxy or hydroxy group in the *para*- position. Additionally, the enol oxygen may be substituted with benzyl or acyl, and this position is substituted with alkyl groups in the instant application. However, the difference in reactivity between an alkoxy or hydroxyl substituted phenyl ring and a phenyl ring would not be considered to be considerable to one skilled in the art. The substituents on the enol oxygen in both the instant application and JACS ’98 serve as protecting groups, of which alkyl and benzyl groups are both able to do. The type of protecting group selected would depend on the type of protection sought, under different reaction conditions .The unsaturated substrates, 4i, are also prepared through a different method, which does not involve reacting a benzaldehyde derivative with a glycolic acid derivative (page 4351, right column, 2nd paragraph). JACS ‘98 is therefore considered to teach the asymmetric hydrogenation of structurally similar compounds.

33. Regarding instant claim 2, JACS ’98 teaches the element of asymmetric hydrogenation.

34. Regarding instant claim 3, JACS ’98 teaches the element of asymmetric hydrogenation.

35. Regarding instant claim 4, JACS '98 teaches that the asymmetric hydrogenation is performed with a chiral catalyst.

36. Regarding instant claim 5, JACS '98 teaches that the chiral catalyst is a transition metal complex.

37. Regarding instant claim 6, JACS '98 teaches that the transition metal complex catalyst is a complex of a metal within Groups 8 to 10 of the periodic table.

38. Instant claim 7 cites that the asymmetric hydrogenation can be performed on a compound of formula (11). JACS '98 teaches that the [(S, S)-Et-DUPHOS-Rh]+ catalyst can be used to perform the asymmetric hydrogenation of compounds similar to formula (11) (Table 3, page 4349, substrates 4a-4k). Instant claim 7 further states that if the transition metal complex is rhodium, the α-alkoxy substituent should be other than acyl. For the substrates listed in Table 3 of JACS '98, the substituent may also be benzyl.

39. Instant claim 8 cites the process of instant claim 7, and also that the transition metal complex is a metal within Groups 8 to 10 of the periodic table. JACS '98 teaches this element.

40. Regarding instant claim 9, JACS '98 teaches that the chiral catalyst is a mixture of a chiral ligand and a transition metal compound.

41. Regarding instant claim 10, JACS '98 does not explicitly teach that the optically active α-alkoxy ester is crystallized from a solvent. However, recrystallization of a product from chosen solvents is a very common procedure to those skilled in the art. It is well known that the purity of compounds can be improved through recrystallization with solvents, and this element is therefore obvious.

42. Regarding instant claim 11, JACS '98 does not explicitly teach that the crystallization solvent is selected from a group consisting of hydrocarbons, alcohols,

ketones, water, and a mixture thereof. However, recrystallization is a commonly known procedure, and the solvents chosen for this depend on the substituents of the compound, among other factors. Hydrocarbons, alcohols, ketones, and water differ from each other in terms of solubility of different compounds, and polarity. It would therefore be obvious to one skilled in the art to possible use different solvents and mixtures thereof for recrystallization of a desired product, and may vary greatly depending on what the exact product is.

43. Regarding instant claim 12, JACS '98 does not explicitly teach that an optically active 3-(4-hydroxyphenyl)propionic acid is crystallized from a solvent. However, this element is obvious as recrystallization is a common process.

44. Instant claim 13 cites the process as stated in instant claim 12, and additionally, that the crystallization solvent is selected from aromatic hydrocarbons, aliphatic hydrocarbons, alcohols, water, and a mixture thereof. JACS '98 does not explicitly teach this element, but it is obvious to one skilled in the art.

45. Regarding instant claim 14, JACS '98 explicitly teaches that phenyl proprionic acids (which are not substituted with an alkoxy or hydroxy substituent in the *para*-position of the phenyl ring) may be prepared by asymmetric hydrogenation. It is obvious to one skilled in the art that this could also be applied to the structurally similar substrates of the instant application.

46. Regarding instant claim 15, JACS '98 does not explicitly teach that an optically active 3-(4-hydroxyphenyl)proprionic acid derivative can be prepared by asymmetric hydrogenation. However, as the substrates that it does specify are structurally similar

and would be expected to have similar reactivity (Table 3, page 4349, substrate 4i), it is obvious to one skilled in the art that this would be applicable to 3-(4-hydroxyphenyl)proprionic acids as well.

47. Regarding instant claim 16, JACS '98 does not explicitly teach that an optically active 3-(4-hydroxyphenyl)proprionic acid derivative could be prepared by subjecting the unsaturated substrate to asymmetric hydrogenation. However, as the substrates that JACS '98 teaches are structurally similar and would be expected to have similar reactivity, it is obvious that this element would apply to 3-(4-hydroxyphenyl)proprionic acids also.

48. Regarding instant claim 17, JACS '98 implicitly teaches that an optically active 3-(4-hydroxyphenyl)proprionic acid derivative is prepared by asymmetric hydrogenation.

49. Regarding instant claim 18, JACS '98 implicitly teaches that an optically active phenylproprionic acid derivative (where the *para*- position of the phenyl ring is substituted with either hydroxyl or an oxygenated protecting group) is prepared by subjecting the unsaturated substrate to asymmetric hydrogenation. JACS '98 does not teach that the unsaturated substrate is prepared by reaction of a benzaldehyde derivative with a glycolic acid derivative.

50. Highly optically pure (R)- and (S)- enantiomers of 3-(4-hydroxyphenyl)proprionic acid derivatives are desirable as precursors and intermediates for a variety of pharmaceutical compounds. US '037 teaches that the unsaturated 3-(4-hydroxyphenyl)proprionic acid can be prepared by reaction of a benzaldehyde derivative with a glycolic acid derivative in the presence of a base, and JACS '98

teaches that the unsaturated phenylproprionic acid derivative can undergo asymmetric hydrogenation with a transition metal-chiral ligand complex to form enantiospecific saturated phenylproprionic acid derivatives.

To obtain the desired highly optically pure *(R)*- and *(S)*- 3-(4-hydroxyphenyl)proprionic acid derivatives, the unsaturated compounds of formula (4) (above) must undergo hydrogenation. As the usual hydrogenation procedures would produce both enantiomers of the desired product, separation by additional methods would be needed to separate out the desired enantiomer product. Asymmetric hydrogenation, as taught in JACS '98, eliminates the need for additional separation methods, as the chiral catalyst selectively hydrogenates one enantiomer of formula (4) over the other. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of US '037 and JACS '98 to arrive at the claims disclosed in the current application.

Claim Rejections 35 USC § 112

51. Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The article *J. Am. Chem. Soc.*, **124**, pgs. 4952-4953, 2002, (known hereafter as JACS '02) is used as an evidentiary reference for the rejection. The examiner

discovered the reference upon a search of the inventive concept and claims of the current application.

52. Claim 1 of the instant application states that an optically active 3-(4-hydroxyphenyl)proprionic acid derivative is prepared by subjecting the unsaturated substrate to asymmetric hydrogenation. In this claim, there is no information given regarding the agent or catalyst to be used for the asymmetric hydrogenation. The specification gives a wide range of possible transition metals, between Groups 8 to 10 of the periodic table, along with an equally wide range of chiral ligands. It is known to those skilled in the art that the ligands and metals used for asymmetric hydrogenation may vary widely depending on the substrates, substituents, and reaction conditions. According to JACS '02, "However, there is no solution in dealing with many transition metal-catalyzed asymmetric transformations since enantioselectivities are often substrate-dependent. Subtle changes in conformational, steric, and electronic properties of chiral ligands can lead to dramatic variations of reactivities and enantioselectivites" (pg. 4952, lines 2-7). The possible substituents of the compound derivatives of formula (4) are extremely broad; for example, the groups for R5-R8 are defined as either independently a hydrogen or a substituent, and R2= alkyl group. Given what is currently known in the art, it does not seem likely that the broad range of possible catalysts in the specification would be equally successful for the asymmetric hydrogenation of the broad possible range of substrates cited in the application. There is also no mention of which specific chiral ligands, or the ligand stereochemistry, that would be used to prepare either the *(R)*- or *(S)*- enantiomer of the phenylproprionic acid derivative product.

Therefore, it would require undue experimentation to determine which specific chiral ligands and transition metals would provide optically active compounds after asymmetric hydrogenation of all the possible substrates in the instant application, and instant claim 1 is rejected.

53. Instant claim 2 cites that an optically active phenylproprionic derivative of formula (4) can be prepared through asymmetric hydrogenation. The possible substrates and chiral ligands and transition metals are not limited, and would also require undue experimentation.

54. Instant claim 3 recites that the 3-(4-hydroxyphenyl)proprionic acid derivative product can be prepared through asymmetric hydrogenation. The substituents are the same as those cited in instant claim 1, and this process would also require undue experimentation.

55. Instant claim 4 cites that the asymmetric hydrogenation would occur with a chiral catalyst. As the possible range of chiral catalysts is not limited to a specific transition metal or ligand, this claim is also rejected as it would require undue experimentation.

56. Instant claim 5 cites that the chiral catalyst is a transition metal complex, but does not limit to a specific transition metal. Rejection of the claim due to requiring undue experimentation also applies.

57. Instant claim 6 cites that the transition metal complex is a complex of the metal of Groups 8 to 10 in the periodic table. As the possible range of catalysts covered by this claim is very large and would require undue experimentation, claim 6 is rejected.

58. Instant claim 7 cites that a compound of general formula (11) undergoes asymmetric hydrogenation with a transition metal complex, with the addition that if the transition metal used is rhodium, the protecting group as represented by R14 in formula (11) is other than acyl. However, since the possible range of R11 and R12 groups remains extremely broad, and the specific type of transition metal to be used for certain substrates is not mentioned, undue experimentation would be necessary.

59. Instant claim 8 cites the process of instant claim 7, and also that, the transition metal complex is a transition metal within Groups 8 to 10 of the periodic table. This claim is also rejected on the basis of requiring undue experimentation.

60. Instant claim 9 cites the process of instant claim 1, and also that, the chiral catalyst is a mixture of a chiral ligand and a transition metal compound. Due to the large possible range of substrates and chiral ligands, this claim is also rejected as it is indefinite and would require undue experimentation.

61. Instant claim 10 states that the optically active product, derived from the asymmetric hydrogenation of a compound of general formula (4), would be crystallized from a solvent. As the possible compounds of general formula (4) are very broad, and recrystallization solvents can vary greatly depending on the specific compound, the claim as states would require undue experimentation.

62. Instant claim 11 cites the process according to instant claim 10, and additionally that, the crystallizing solvent is selected from hydrocarbons, ketones, alcohols, water, and a mixture thereof. As the possible compounds of general formula (4) are very broad, it would be reasonable to expect that not every hydrocarbon, ketone, alcohol,

water, or a mixture thereof would be a successful recrystallizing solvent for all of those possible compounds. Rejection due to requiring undue experimentation applies.

63. Instant claim 12 cites the process according to instant claim 1, and also that, the optically active 3-(4-hydroxyphenyl)proprionic acid derivative product (after asymmetric hydrogenation) would be obtained by crystallization from a solvent. As the possible derivatives are very broad, undue experimentation would be required to determine which solvent or mixture would be successful for each compound.

64. Instant claim 13 cites the process according to instant claim 13, and also that, the crystallization solvent is selected from a group of aromatic hydrocarbons, aliphatic hydrocarbons, alcohol, water, and mixture thereof. Undue experimentation would also be necessary to carry out the process according to this claim.

65. Instant claim 14 cites the process in which the compound of general formula (4) undergoes asymmetric hydrogenation. As the possible range of compounds from this formula are very broad, undue experimentation would be necessary to determine which catalyst-chiral ligand combination would be successful for specific compounds.

66. Instant claim 15 cites the process for preparing an optically active 3-(4-hydroxyphenyl)proprionic acid derivative, by performing asymmetric hydrogenation on a compound of formula (4). As the possible compounds of formula (4) are broad, and the possible hydrogenating catalysts are also very broad, rejection due to requiring undue experimentation applies.

67. Instant claim 16 recites claim 15. There is a difference between the starting compound for both claims, as the phenylproprionic acid derivative of claim 15 has the

phenyl ring oxygen substituted by a protecting group. The final product for both claims is the saturated, deprotected 3-(4-hydroxyphenyl)proprionic acid derivative. The rejection as stated for instant claim 15 also applies.

68. Instant claim 17 recites instant claim 15, and the rejection due to the same reasoning applies.

69. Instant claim 18 recites that a compound of formula (4) is prepared by reaction of a benzaldehyde derivative with a glycolic acid derivative, which further undergoes asymmetric hydrogenation, and deprotection to form the saturated 3-(4-hydroxyphenyl)proprionic acid derivative. As the possible range of substituents is the same as in instant claim 1, the possible substrates of this general formula is very broad. Undue experimentation would be required to determine the catalysts that would be used for the asymmetric hydrogenation of each substrate.

70. The information disclosure statement (IDS) submitted on 5/10/06 was filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached on Monday-Thursday 7:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on (571)272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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S.P.

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